UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,994	08/03/2001	Michael R. Bowman	GIN-5381	7090

7590 07/14/2003

FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112-3801

EXAMINER
FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/921,994	BOWMAN, MICHAEL R.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,12,16,17 and 24-29* is/are pending in the application.

4a) Of the above claim(s) *7, 12, 16, 17, 28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

1. Claims 1-7, 12, 16, 17, 24-29 are pending.

Claims 1-6, 24-27 are rejected.

Claims 7, 12, 16, 17, 28 and 29 are withdrawn from consideration.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Election/Restrictions

2. Applicant's amendment to claim 7 does not change its Group II status and claim 28 is drawn to the same non-elected group as claim 7 and is therefore withdrawn. Claim 29 is drawn to non-elected Group III and is also withdrawn. Applicant correctly notes that upon indication of allowable subject matter, these non-elected claims would be rejoinable under Ochiai.

Specification

3. The objection to the disclosure is withdrawn in view of the amendment to the specification.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-6 and 24-27 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of nucleic acids termed EBI-3-alt in the specification and are further defined by reference to SEQ ID Nos: 1-3. An important point is that while the name of the protein is EBI, reminiscent of Epstein Barr induced, there is no evidence found in the specification that the current nucleic acid or protein are induced by infection of cells with Epstein Barr virus. Thus, no utility can be based upon this inference since there is no apparent evidence that this protein is, in fact, induced by Epstein Barr virus.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The only cited utilities identified by the examiner are to detect the EBI-3-alt nucleic acid or protein itself, to make antibodies and to screen drugs. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the protein. No well established utilities for this specific EBI-3-alt protein are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, the evidence in the specification itself teaches that the EBI-3-alt is homologous both to a cytokine receptor and to a nitrous oxide reductase (see page 65, lines 27-36 of specification). This

extreme disparity in possible activities for the protein highlights the absence of any substantial utility.

As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials). There is no data in the specification linking this gene to any disease or to any specific biological function. The only element known is that the protein may be induced by the Epstein Barr virus, but this provides no substantial utility and no evidence that this induction occurs was found in the specification. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, there is no suggestion for any particular use of the EBI-3-alt nucleic acids as distinguished from any other nucleic acid which encodes an open reading frame. The current specification simply recites a laundry list of every possible generic use to which a nucleic acid and the protein encoded by that nucleic acid could be put. However, there is not a single substantial use related to the EBI-3-alt protein or nucleic acid itself.

Specific Utility

Further, none of the laundry list of utilities identified in the specification are specific to the EIB-3-alt protein or nucleic acid. As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure

of what condition can be diagnosed". Here, there is not even such a general prediction. There is no disclosure of any condition which can be diagnosed and hence, no specific utility. In particular, there is no evidence that the protein or nucleic acid are induced by Epstein Barr virus. There is no disclosure of any utility whatsoever which can be performed by the EBI-3-alt protein or nucleic acid which is specific to those molecules and which could not be performed using any nucleic acid or protein that exists.

Finally, with regard to the utility analysis, the current situation directly tracks Example 4 of the utility guidelines, where a protein of entirely unknown function was characterized as lacking utility.

Response to Arguments – 101 Rejection

6. Applicant's arguments filed April 21, 2003 have been fully considered but they are not persuasive.

Applicant argues that a 99.3% identity to EBI over a region of approximately 700 nucleotides provides utility for the current claims. Contrary to Applicant's assertion, the credibility of the utilities suggested are not at issue. This issue is whether these utilities are sufficiently substantial and specific to warrant the grant of a patent. Applicant's argument is not found persuasive for several reasons.

First, the reliance on the identity underlies the fundamental problem in this application. The identity is not, as Applicant states, to an Epstein Barr virus component, but rather to a human nucleic acid, EBI-3. As noted in the rejection, the homology is to two entirely different types of protein, one of which is a cytokine receptor and the other of which is a nitrous oxide reductase. There is no evidence or teaching that the actually

protein has either of those activities. Further, with regard to EBI-3 itself, the only disclosed utility for this protein is that it is induced by the Epstein Barr virus. Activation of proteins is well known to be exquisitely sensitive and specific, with different allelic variants being activated at different times in cell cycle, in development or in response to extracellular events. This differential expression is appreciated by the specification itself, at page 31, lines 1-14, where the specification recognizes "tissue specific" regulatory sequences. Therefore, there is no reason to believe that simply due to some level of homology, the current protein is activated by Epstein Barr virus or would serve as a marker for that virus.

Second, Applicant relies upon a 1978 text, (not submitted) and a 1997 paper (not submitted) as well as the utility guidelines to support the point that homology alone is predictive of utility. As noted in the enablement rejection below, a 2001 paper shows that homology is not predictive of function in many instances and provides evidence of such an instance. Also, this argument is not persuasive because it fails to address the central question. Homology, as in the case of ligases, may be predictive, where there are known domains in the protein with known properties which yield known enzymatic effects. This situation is not like the ligase example, but is much more similar to Example 12 of the Guidelines, where a "receptor" was found not to have utility because there was no real world context of use for the receptor. In the current case, unlike the guideline example, we do not even have the receptor itself. EBI-3 would be the receptor the guidelines would address. Here we simply have a protein that is

homologous to the receptor. This protein has no utility because there is no known "real world" use for the protein. Applicant has not provided any such "real world" use.

Applicant further argues that there is a "well established" utility as a research tool. This argument is not persuasive because there is no such utility identified in the art for unknown nucleic acids which encode unknown proteins. As the guidelines note "well established" utility does not encompass nonspecific utilities that would apply "to virtually every member of a class of materials, such as proteins or DNA (see Utility guidelines, page 7).

For these reasons, the utility rejection is maintained.

Claim Rejections - 35 USC § 112 - Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to nucleic acids which encode the EBI-3-alt protein. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass a variety of nucleic acids which may encode the EBI-3-alt protein, including alternatively spliced variants, nucleic acids which encode related proteins and a variety of mismatches based upon the 75% homology language. An important point is that while the name of the protein is EBI, reminiscent of Epstein Barr induced, there is no evidence found in the specification that the current nucleic acid or protein are induced by infection of cells with Epstein Barr virus. Thus, no utility can be based upon this inference since there is no apparent evidence that this protein is, in fact, induced by Epstein Barr virus.

Quantity of Experimentation

The quantity of experimentation in this area is very large since there is significant variability in the effect and function of proteins in living organisms. It is a truism that

each protein has a different function in the cell and in the current situation, no use has been identified for the EBI-alt-e protein. Thus, in order to make any use of the protein, it's function in the cell must first be identified. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The prior art contains no precise match for the EBI-3-alt protein and therefore the protein and nucleic acid cannot be enabled based upon prior art disclosures. Birkenbach teaches a sequence which has significant homology with the EBI-3-alt nucleic acid (it is noted that that patent issued prior to the current utility guidelines). The homology evidence presented in the specification indicates a relationship with two extremely divergent proteins, one a chemokine receptor and the other an enzyme involved in sulfur metabolism. Thus, the ordinary practitioner would have no expectation regarding the function of the EBI-3-alt protein and nucleic acid. It is extremely unpredictable what function a protein or nucleic acid will have, even when there is very good homology data. For example, Thrower et al (Trends Pharm. Sciences (2001) 22 (11) 580-6) notes regarding some inositol receptors that "Although these receptor isoforms possess high homology, interesting differences in their Ca2+ dependence, Ins(1,4,5)P3 sensitivity and subcellular distribution exist, implying distinct cellular roles. (abstract)". Thus, even where there is extremely high sequence homology, the proteins may have distinct physiological roles. In the current case, where the homology is lower and is related to two extremely divergent types of proteins, the physiological role is significantly unpredictable.

Working Examples

The specification has no working examples which disclose the function of the EBI-3-alt protein or nucleic acid.

Guidance in the Specification.

The specification has an abundance of generic guidance regarding uses for the EBI-3-alt protein and nucleic acid, but lacks any specific or substantial use. There is no disease or condition identified which is associated with this protein or nucleic acid, there is no physiological or cellular role identified for this protein or nucleic acid and there is no function whatsoever which has been associated with the EBI-3-alt protein or nucleic acid.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to use the product of the claim as broadly written.

Response to Arguments – Enablement

8. Applicant's arguments filed April 21, 2003 have been fully considered but they are not persuasive.

Applicant argues that the amendment to delete fragments overcomes this rejection. This argument is not persuasive because the issue is use of the product, and the claims still have no patentable use. Therefore, the enablement rejection is maintained.

Claim Rejections - 35 USC § 112 – Written Description

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-6, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register:

December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID Nos 1-3. Thus, applicant has express possession of only the specific EBI-3-alt sequence, in a genus which comprises hundreds of millions of different possibilities based upon the fragment and 75% or 60% homology language. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at

> 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the percent homology or fragments of EBI-3-alt lack any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "60% homologous to the amino acid sequence of SEQ ID NO: 2", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a deletion, without any definition of the particular alterations based upon the fragments or homology claimed. In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Response to Arguments – 112 written description Rejection

11. Applicant's arguments filed April 21, 2003 have been fully considered but they are not persuasive.

Applicant's amendments do not overcome the issues with regard to the percent homology and allelic variation permitted by these claims. With regard to the argument that the claims are original and therefore constitute their own description, MPEP 2163 notes "However, as discussed in paragraph I., supra, the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention."

MPEP 2163 further notes "A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." That is the precise situation here, where the claim using homology language is entirely functional, without any structural correlation to the specific sequence. Therefore, the written description rejection is maintained.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 3-6, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Birkenbach et al (U.S. Patent 5,744,301).

Birkenbach teaches an isolated nucleic acid which comprises a region that is 75% homologous to SEQ ID NO: 1 (see SEQ ID NO: 5 at columns 47-50 and alignments attached where SEQ ID NO: 5 has a region of 99.3% local similiarity) as well as comprising a fragment of more than 30 nucleotides of SEQ ID NO: 1 (see SEQ ID NO: 5 at columns 47-50 and alignment attached). Birkenbach further teaches placement of the sequences into an expression vector which may include heterologous seuqences (see column 8, lines 55-67) and which may be placed into host cells (see column 8, lines 40-50). Birkenbach expressly teaches the use of mammalian host cells (see column 16, lines 16-25). Finally, Birkenbach expressly teaches placement of nucleic acids into a kit format for detection purposes (see column 13, lines 45-67).

Response to Arguments – 102 Rejection

14. Applicant's arguments filed April 21, 2003 have been fully considered but they are not persuasive.

Applicant argues that the rejection is mooted by the amendment. However, claim 1 still encompasses "allelic variants." The sequence of Birkenbach is inherently an "allelic variant" of the claimed sequence and therefore the prior art rejection remains applicable.

Therefore, all of the rejections are maintained.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634

July 14, 2003